PTO: 2003-5832

Japanese Published Unexamined Patent Application (A) No. 58-079915, published May 13, 1983; Application Filing No. 56-178368, filed November 9, 1981; Inventor(s): Hidenori Kosawa et al.; Assignee: Nippon Soda Corporation; Japanese Title: Manufacturing Method for Elongated Chemical agents

---

MANUFACTURING METHOD FOR ELONGATED CHEMICAL AGENTS

CLAIM(S)

1) A manufacturing method for an elongated chemical agent, whereby water-soluble high polymer, chemical agent, and additive, if needed, are evenly mixed and this admixture is formed by melt-extrusion molding to produce an elongated chemical agent.
2) A manufacturing method for an elongated chemical agent, as cited in Claim 1, wherein the water-soluble high polymer is hydroxyl propyl cellulose.

DETAILED DESCRIPTION OF THE INVENTION

The present invention pertains to an improved manufacturing method for elongated chemical agents. Recent years, elongated chemical agents have been developed as a medicine for local treatment for the following reasons: 1) The medical effect can be enhanced deep in the tissues; 2) The

medicine can directly attack the diseased area; 3) Once it can be locally applied, a side effect on an entire body can be reduced.

As to the prior art manufacturing method for elongated chemical agents, a pressure molding method (Chem, Pharm, Bull, 28 (4) 1125 –1130 (1980) is well known. This method, however, comes with the following problems: 1) The molding device (molds) is not easy to develop; 2) The needle-shaped medical product has a narrow diameter, so the needle-shaped tablet is hard to remove from the molding device since it tends to be broken or cracked; 3) When many different types of chemical agents are used, streaks of chemical agents are created.

The inventors of the present invention, after having assiduously studied to eliminate the aforementioned problems, found that the objective of the present invention can be accomplished by manufacturing the needle-shaped chemical agents by a melt-extrusion molding method, and have produced the present invention.

The present invention presents a manufacturing method for enlongated chemical agents, wherein water-soluble high polymer, chemical agent, and an additive, if desired, are evenly mixed and this admixture is shaped into an elongated tablet by a melt-extrusion molding method.

The water-soluble high polymer used in the present invention is the base material of the elongated chemical agent, and a natural or synthetic water-soluble one can be used as long as it does not negatively affect a human or animal body. For example, the following can be cited as the applicable water-soluble high polymers: hydroxyl propyl cellulose (herein after referred to as HPC); methyl cellulose; hydroxyl propyl alkyl cellulose; carboxyl methyl cellulose or water-soluble cellulose derivative such as its salt; polyacrylic acid or its salt; carboxyl vinyl polymer; soda alginate; but HPC is particularly preferred.

As to the chemical agents, they are medicines or animal medicines having a curing or preventive effect. For example, the following can be cited:

1) Antibiotics

Chemical agents in penicillin group, e.g., Ampicillin and sulpenicillin; chemical agents in cephem [spelling assumed for not being able to locate in dictionaries] group, e.g., cephalothin; chemical agents in aminoglycoside group, e.g., gentamicin, kanacycin; chemical agents in tetracycline group, e.g., oxytetracycline, tetracycline; chemical agents in macrolide group, e.g., erythmycin.

2) Anticancer agents

Alkylation agents, e.g., karubokon [Transliteration was produced for not being able to locate in dictionaries.]; pyrimidine antimetabolites, e.g., fluorouracil; antibiotics, e.g., bleomycin, mitmycin; purine antimetabolites, e.g., thionoicy [spelling assumed]; alkaloid agents.

3) Others

Sulfur agents, e.g., sulfdimetoxine, sulfmetoxazole; hemostatic agents; steroid agents.

As to the additive used in the present invention, a proper amount can be added to adjust the hardness of the agent for adjusting the elution speed of the agent or depending upon its purpose. For example, they are: moisture-repellent high polymer compounds, such as ethyl cellulose and shellac; inorganic compounds such as talc and titanium oxide. Moreover, an extender, flavor, deodorant, and coloring agent may be added if necessary.

When the chemical agents of the present invention are produced, said water-soluble high polymer, chemical agent, and additive, if needed, are mixed by the prescribed amount for each in a bowl and thoroughly blended by an ordinary means. If necessary, the admixture may be once formed into slugs and then crushed. This admixture is put in a heated melt-extrusion molding device and melted at 100 - 200°C. Subsequently, pressure is applied from above at 50-300 kg/cm^2, and the admixture is extruded from

the 0.5 – 3 mm ø hole underneath. At the same time, the molded product being extruded is pulled by the force of 0 – 15 kg/cm^2 to produce the prescribed elongated chemical agents.

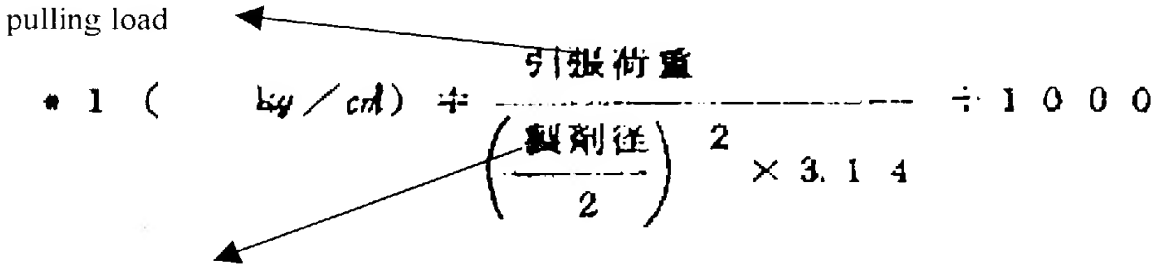
The present invention is further explained below with reference to the embodiment example, but the product of the present invention is not limited to this example.

(Embodiment Example 1)

HPC 4.5 parts/weight and fluorouracil 0.5 parts/weight are evenly blended in a bowl. This admixture is partially put to compression molding using an ordinary 10 mm ø die to produce a 10 mm ø x 10mm cylindrical tablet. This tablet is put in the melt-extrusion molding device heated to 150°C (Flow Tester 301 made by Shimazu Manufacturing Engineering, Inc.) and left alone for 10 minutes. Then, load of 100 kg was exerted to extrude it from the die having a 1 mm ø nozzle diameter, while simultaneously pulling it by the weight of 80g (10.2 kg/cm^2) to produce a 1 mm ø elongated chemical agent.

By using the same process steps as those in the embodiment example 1, excellent elongated agents were produced, and the result is summarized in Table 1.

Examples	Component (parts/weight)			Melt temperature (°C)	Extrusion load (kg)	Pulling load (g)	Used nozzle diameter (mm)	Product diameter (mm)
	Water-soluble high polymer	Chemical agents	Additives					
2	HPC (2.5)	Ampicillin (2.5)	-	138	150	20y[*1] (1.1 kg/cm^2)	1.5	1.5
3	HPC (4.95)	Gentamicin (0.05)	-	140	100	20 (0.5)	2.0	2.2[*2]
4	HPC (4.95), soda polyacrylate 4.95	Bleomycin (0.1)	-	174	200	20 (2.5)	1.5	1.0
5	Same as the above	Adriacin (0.1)	-	176	150	20 (1.1)	2.0	1.5
6	HPC (2.5), soda polyacrylate (20)	Dorakisamu [translateration] acid (5.0)	Talc (0.5)	176	200	20 (2.5)	1.5	1.0
7	Same as the above	Sulfisomycin (1.0)	Same as the above	175	200	20 (1.1)	2.0	1.5



*2: Slightly expanded after the extrusion.

Translations
U. S. Patent and Trademark Office
10/17/03
Akiko Smith